

REMARKS

The undersigned attorney apologizes for the informality in the previous amendment. In transferring the claim listing into the document claims 1-44 were deleted (as they are no longer in prosecution), but the attorney neglected to insert an indication of their cancellation.

In the Office Action the Examiner makes a new rejection of the claims under 35 USC § 112, first paragraph for failing the Written Description requirement. It would appear that the Examiner is focused on the word "directly" in the claim. The Examiner states that the specification contained only the disclosure of paragraph [0087] concerning the word "directly." Applicant is not aware that the requirements of 35 USC § 112, first paragraph—specifically the written requirement demonstrating the possession of the invention hinges on the presence or description of a word found in a claim—unless, perhaps, that word is an unusual or specialized word that requires support in the specification. Applicant respectfully submits that "directly" is not such a word. Claim 45 was earlier amended to bring attention to a method for topically killing and inhibiting both bacteria and fungi. It is submitted that the claim is, therefore, directed to the use of an ACQA for killing bacteria and fungi. The question then, whether the specification as filed contains data that would lead one of ordinary skill in the art to believe that the inventor had possession of the invention (namely that ACQA can be used to kill fungi and bacteria). If the specification contains such data, then the written description requirement of possession of the invention is met. The Examiner has quoted the "immediately envisage" test from *Fujikawa v. Wattanasin*. Applicant respectfully submits that one of ordinary skill in the art would be aware of the myriad uses of ACQAs for treatment of excessive sweating; however, at the time the instant specification was filed one of ordinary skill in the art did not know that ACQAs at concentrations used for excessive sweating were also efficacious at killing and inhibiting both bacteria and fungi. When presented with test data showing such activity, one of ordinary skill in the art would immediately envisage the claimed invention.

A further 35 USC § 112, first paragraph requirement is that of enablement. The enablement question turns on assuming that the inventor did have possession of the invention (namely, that ACQA can effectively kill and inhibit bacteria) does the specification enable one of ordinary skill in the art to practice the invention. As will be described more fully below, the specification and the incorporated by reference co-pending application contain abundant details on the formulation, application and testing of ACQA containing compositions for the amelioration of sweating and malodor associated therewith. Assuming that the specification demonstrates that certain concentrations of ACQAs kill and inhibit bacteria and fungi, it would be trivial for one of ordinary skill in the art to use the disclosed formulations with the goal of not only reducing wetness and malodor but of actually killing bacteria and fungi. Thus, the enablement prong of 35 USC § 112, first paragraph is also met.

Applicant again directs the Examiner to paragraphs [0055] to [0060]. Paragraph [0058] indicates that ASTM Protocol #1891-97 was used to determine the MIC and D values for ACQAs against common pathological fungi and bacteria that would be found on the skin. One of ordinary skill in the art would immediately understand the impact of the ASTM Protocol studies and their significance. Previously, glycopyrrolate was not known to be a microbial inhibitor or microbicide. The reported tests show that the D value against the dermatophyte *Trichophyton mentagrophytes* was 24 minutes while the D value for the application vehicle was essentially insignificant (215 minutes) because the vehicle would be expected to evaporate before 215 minutes had passes. The MIC activity was in the range of >0.1%--a very respectable level of activity. This would cause one of ordinary skill in the art to expect an application of glycopyrrolate to be effective at controlling this fungus. Paragraph [0060] reports that other ACQAs show significant activities against a pathogenic yeast (*Candida albicans*) as well as a mold (*Aspergillus niger*). These results would cause one of ordinary skill in the art to understand that the ACQA effect extended not only to compounds other than glycopyrrolate but also to fungi other than the dermatophyte *Trichophyton* (one of ordinary skill in the art would also recognize that *C. albicans* is an important human pathogen).

Paragraphs [0061] – [0063] expand these observation to bacteria in addition to fungi. One of ordinary skill in the art would be impressed that when tested against skin bacteria that can be pathogenic, glycopyrrolate shows a D value of only 4 minutes and MIC values in the range of 0.1 to 1%. This would cause one of ordinary skill in the art to understand that topical application of ACQAs at the concentrations reported would be effective for killing and inhibiting bacteria on the skin (it being demonstrated elsewhere in the specification that these concentration are free of serious side effects). Applicant considers that the Examiner may not be fully aware of what these results would mean to one of ordinary skill in the art because even though the Examiner is undoubtedly very familiar with this art, it seems unlikely that the Examiner has memorized the D values of various compounds. For this reason Applicant submits herewith a contemporaneous (published 17 October 2003) research article explaining D value testing and showing D values for some common bacteria and well-known sterilizing solutions (BMC Infectious Diseases 2003, 3:24). This article demonstrates (see Fig. 1) that the D values for a range of bacteria exposed to the common hospital surface sterilant 2% glutaraldehyde are in the range of 4-6 minutes. One of ordinary skill in the art would never apply glutaraldehyde as a topical treatment for body odor but would likely be impressed that 3% glycopyrrolate shows a D value (4 minutes) similar to 2% glutaraldehyde. Applicant respectfully submits that faced with these results one of ordinary skill in the art would conclude that Applicant was in possession of a method to kill and inhibit both bacteria and fungi.

Claim 45 has now been amended to clarify the point that the claimed method of killing and inhibiting bacteria by contact with the effective substance (e.g., by means of topical application) since the specification does not support claims to parenteral applications.

In the Office Action the Examiner repeated the rejections of claims 45-49 under 35 USC § 103(a) as being unpatentable over **Wassenaar** (U.S. Patent No. 7,060,289) in view of the Merck Manual. Essentially, the Examiner observes that the Merck Manual

teaches that athlete's foot, a fungus infection, commonly grows in warm moist areas between the toes. Further although **Wassenaar** does not teach a method for killing or inhibiting microorganisms including fungi, **Wassenaar** does disclose a single case study of a patient wherein excessive sweating of the forehead and groin resulted in a constant facial rash and chronic fungal infection of his groin. After **Wassenaar** used an anticholinergic amine to reduce the sweating, the facial rash and fungal groin infection improved. Therefore, the Examiner concludes that the combination of the Merck Manual (fungal infections develop in warm moist locations) with **Wassenaar** (excessive sweating may lead to fungal infections and reduction of such sweating causes improvement in the fungal infection) makes it obvious to use anticholinergic amines to inhibit and kill microorganisms including fungi.

Applicant respectfully traverses the Examiner's obviousness finding. The experiment reported by **Wassenaar** possibly demonstrates that reducing the availability of moisture (sweat) can lead to improvement in a facial rash and fungal groin infection. Epidermal rashes can be ameliorated by a variety of agents including hydrocortisone. Further, it is not clear from the description in **Wassenaar** that fungus was at all involved in the rash. Absent a showing (as in the present application) of actual killing or inhibition of fungi, one of ordinary skill in the art would not interpret **Wassenaar** as showing or suggesting killing and inhibition of fungi. Rather the experiment suggests that reducing the level of moisture helps control a fungal groin infection. This experiment does not demonstrate or suggest that ACQAs (such as glycopyrrolate) kill and inhibit microorganisms including dermatophytic fungi. By "killing" one means that the compound has a direct toxic biological effect as opposed to an indirect environmental effect such as by altering the growth environment (i.e., making things drier). Applicant has made the hitherto unknown and unexpected discovery that ACQAs, including glycopyrrolate kill (D-value) and inhibit (MIC) fungi and bacteria in tests. Again the Examiner is directed to paragraphs [0057] to [0063] of the specification. It is known that anti-fungal agents are widely sought; Applicant is the first to recognize the anti-fungal properties of this class of compounds. Applicant also recognizes the association of

fungal pathologies with warm and moist environments (see paragraph [0086]) pointed out by the Examiner and exemplified by Experiment 1 of **Wassenaar**. The killing and inhibition of microorganisms, including fungi, by ACQAs above and beyond inhibition due to a moisture reducing effect was not known in the art and is not obvious in face of any of the cited art.

While it might be obvious to inhibit the growth of microorganisms by reducing the level of moisture (sweat) available in the growth environment (**Wassenaar**) Applicant respectfully points out that it was not obvious and was entirely unexpected to employ ACQAs as an agent to kill and inhibit fungi and bacteria. As shown in the Merck reference cited by the Examiner fungal infections (tinea corporis) can occur at any site on the body. Scalp and nail infections are pointed out as being particularly difficult to treat. Therefore, it is apparent that fungal infections are common on areas of the body that are generally not particularly moist. As demonstrated by Applicant's *in vitro* tests, ACQAs do kill and inhibit fungi (*Trichophyton*, a pathogen mentioned in the reference, was used in those tests). The ability of Applicant's inventive method to kill and inhibit fungal pathogens and bacteria on dry parts of the body would not have been obvious in light of any of the cited prior art. Therefore, Applicant respectfully requests the Examiner to withdraw the rejections under 35 USC § 103 in view of **Wassenaar** be withdrawn.

Applicant respectfully suggests that the prior art does not anticipate or render obvious the use of ACQAs to kill and inhibit fungi and bacteria. On page 9 of the Office Action the Examiner points out that "Products of identical chemical composition (i.e. glycopyrrolate) can not have mutually exclusive properties." The Examiner then cites *In re Spada*. Applicant respectfully contends that this citation is inapposite. In *re Spada* is directed towards novelty of a composition and the property of "inherency" in destroying the novelty of a compound. Certainly, the discovery of the antifungal properties of a known compound cannot render that compound novel for patentability purposes. However, U.S. patent laws clearly allow the patentability of a new use for an old compound. That is clearly the case with the method claimed here. The prior art was not

aware that ACQAs were effective at both killing and inhibiting fungi and bacteria. Therefore a method of employing ACQAs to kill and inhibit fungi and bacteria is patentable.

Finally, in rebutting Applicant's previous arguments the Examiner points out that the features on which the Applicant relies are not recited in the claims. Applicant presumes that this is a reference to the claims' possible parenteral coverage (application to an "area") while the tests and formulations were directed to a topical application. That has been corrected in the above claim amendments.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested. If for any reason the Examiner still finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (310) 229-9928 to discuss the steps necessary for placing the application in condition for allowance. You are hereby authorized to charge any fees due and refund any surplus fees to our Deposit Account No. 22-0261. Please reference matter number 94902-256172.

Respectfully submitted,

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Date: 2 April 2009

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